- (a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module;
- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;
- (c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;
- (d) identifying a bi-ligand that binds to and has specificity for said enzyme; and
- (e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.
- 11. The method of claim 9, wherein said enzyme in said enzyme family is an enzyme selected from the group consisting of a kinase, dehydrogenase, oxidoreductase, GTPase, carboxyl transferase, acyl transferase, decarboxylase, transaminase, racemase, methyl transferase, formyl transferase, and  $\alpha$ -ketodecarboxylase.
- 12. The method of claim 9, wherein said enzyme family binds a cofactor selected from the group consisting of

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nicotinamide adenine dinucleotide, nicotinamide adenine dinucleotide phosphate, thiamine pyrophosphate, flavin adenine dinucleotide, flavin mononucleotide, pyridoxal phosphate, coenzyme A, tetrahydrofolate, adenosine triphosphate, guanosine triphosphate and S-adenosyl methionine.

- 13. The method of claim 9, wherein said linker has approximate C2 symmetry.
- 14. The method of claim 13, wherein said linker has perfect C2 symmetry.
- 37. The method of claim 9, wherein steps (c) and (d) are repeated to identify a bi-ligand that binds to and has specificity for a third enzyme in said enzyme family.

Please add the following new claims.

- 38. (New) A method for identifying a population of bi-ligands to dehydrogenases in a dehdrogenase enzyme family, comprising:
- (a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of a dehydrogenase in said dehydrogenase enzyme family, to form a module;

- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;
- (c) screening said population of bi-ligands for binding to a dehydrogenase in said dehydrogenase enzyme family;
- (d) identifying a bi-ligand that binds to and has specificity for said dehydrogenase; and
- (e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second dehydrogenase in said dehydrogenase enzyme family.
- 39. (New) The method of claim 38, wherein said expansion linker has approximate C2 symmetry.
- 40. (New) The method of claim 38, wherein said expansion linker has perfect C2 symmetry.
- 41. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising:
- (a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module, wherein said enzyme family binds nicotinamide adenine dinucleotide;

- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;
- (c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;
- (d) identifying a bi-ligand that binds to and has specificity for said enzyme; and
- (e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.
- 42. (New) The method of claim 41, wherein said expansion linker has approximate C2 symmetry.
- 43. (New) The method of claim 41, wherein said expansion linker has perfect C2 symmetry.
- 44. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising:
- (a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module, wherein said enzyme family binds nicotinamide adenine dinucleotide phosphate;

- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;
- (c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;
- (d) identifying a bi-ligand that binds to and has specificity for said enzyme; and
- (e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.
- 45. (New) The method of claim 44, wherein said expansion linker has approximate C2 symmetry.
- 46. (New) The method of claim 44, wherein said expansion linker has perfect C2 symmetry.
- 47. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising:
- (a) attaching a linker to a common ligand, wherein said common ligand competes for cofactor binding, wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module;

- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;
- (c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;
- (d) identifying a bi-ligand that binds to and has specificity for said enzyme; and
- (e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.
- 48. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising
- (a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module, wherein said enzyme family comprises two or more enzymes that bind to the same cofactor;
- (b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;